JOBNAME: ajo 26#2 2005 PAGE: 1 OUTPUT: Thu February 17 11:33:00 2005
lww/ajo/93636/MAO148898

Otology & Neurotology
26:237–240 © 2005, Otology & Neurotology, Inc.

Hereditary Bilateral Conductive Hearing Loss Caused by Total Loss of Ossicles: a Report of Familial Expansile Osteolysis

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Objective: The objective of this study was to report on three members of a family with familial expansile osteolysis; the important point about these patients was that none of them had middle-ear ossicles.
Study Design and Subjects: A retrospective case review including three cases with familial expansile osteolysis.
Setting: Department of Otolaryngology in a tertiary referral center.
Interventions: Each patient underwent computerized tomography of the temporal bone in the coronal view, audiometric and tympanometric evaluations, biochemical investigation, whole body isotope scans by Tc-99 mMDP and X-ray. Also the patients' pedigree was studied. Two of the patients had exploratory middle-ear surgery as well.
Results: The temporal-bone computed-tomography scan in the coronal view of all three patients and also exploratory middle-ear surgery, which was done on two of the patients, showed no ossicles in the middle ear of either ear in all three cases. This feature hadn't been reported in previous studies. Hearing loss was revealed in the medical histories since childhood. Audiometry indicated mild to moderate conductive and mixed hearing loss and also an AD-type tympanogram pattern along with an absence of acoustic reflexes in both ears of the cases. Both serum alkaline phosphatase and hydroxyproline levels were elevated. There was an increase in uptake and activity at multiple foci of the whole skeleton. No improvement in hearing thresholds was obtained after reconstruction of the middle ear.
Conclusion: The total absence of middle-ear ossicles can probably be regarded as a new symptom in some patients with familial expansile osteolysis. Common ossiculoplasty for improving the hearing thresholds in this condition may be unsuccessful; therefore, both surgeons and patients must be completely aware of the contingent undesirable results.
Otol Neurotol **26:**237–240, 2005.

Familial expansile osteolysis (FEO) was first reported in 1988 by Osterberg et al. (1). They described a large family from Northern Ireland who had an autosomal-dominant bone dysplasia, which, while exhibiting some histological similarity to Paget disease, was distinct enough in its features and natural history to be recognized as a separate condition. Over 40 individuals of five generations of the Northern Irish family were affected. Many patients in the family had suffered pathological fractures, severe bone pain, and eventually major limb amputations (1–3). Most affected persons showed deafness that initially was conductive but might have later become mixed conductive and sensorineural in type. The onset of deafness was usually before the age of 10 years. Typically in FEO, serum alkaline phosphatase and urinary hydroxyproline are elevated. Whole body isotope scans by Tc-99 mMDP usually reveal increased uptake and activity at multiple foci of the whole skeleton. Other symptoms of this disease are spontaneous necrosis of the long process of the incus and an abnormal stapedial footplate (4,5). FEO is associated with extensive, external resorption affecting the cervical and apical areas of permanent teeth. Permanent tooth-root resorption leads to pain, mobility, fracture, and ultimately tooth loss. Reduction in the size of the pulp chamber and root-canal system are another findings in

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FEO (6–8). FEO is an autosomal-dominant disorder that results from an insertion mutation in the *TNFRSF11A* gene (9). Previous linkage studies mapped the gene responsible for FEO to an interval of less than 5 cM between D18S64 and D18S51 on chromosome 18q21.2–21.3 in a Northern Irish family (10).

CASE REPORTS

The patients presented in this case study are three members of a family with FEO, a 47-year-old man and his two children; a 15-year-old daughter and an 11-year-old son. They were referred to the Otology Clinic of Rasool Akram Hospital, Iran Medical University. A preliminary study of the family's medical history led to the hypothesis that the patients are affected with FEO. To achieve a precise diagnosis, a computerized tomography (CT) scan of the temporal bone in the coronal and axial views, audiometric, genetic, dental, and biochemical investigations, and whole body isotope scans by 99Tc mMDP and x-ray were done. Finally, the obtained data confirmed the presence of FEO in all three cases. Two of them underwent exploratory middle-ear surgery; also an ossiculoplasty was done to improve their hearing thresholds.

The pedigree of this family had six affected members in three generations with hereditary autosomal dominant pattern (Fig. 1).

CASE 1

Case 1 was a 47-year-old man. Investigation of his family history revealed FEO in his mother, brother, and also his children. Study of his medical history indicated a bilateral hearing loss and tinnitus since childhood. His audiogram at the age of 20 showed mild, bilateral, conductive hearing loss. The last audiogram indicated a moderate to severe, bilateral, mixed hearing loss. The air–bone gaps in low and high frequencies were both 55 dB in the right ear. In the left ear the air–bone gaps in low and high frequencies were 35 and 25 dB respectively. Impedance testing revealed a high compliance in middle ears (type AD) and also absence of acoustic reflexes in both ears. CT scan in coronal view showed no ossicles in the middle ear of either ear (Fig. 2) and whole body isotope scans by Tc-99 mMDP revealed increased uptake and activity in multiple foci of the whole skeleton. The onset of his loss of dentition coupled with long-bone pain started at 10 years of age. Both serum alkaline phosphatase and hydroxyproline levels were elevated in the biochemical investigation. This patient was offered ossiculoplasty for improvement of hearing thresholds, but he decided not to undergo the surgery. He was referred for fitting with digital hearing aids.

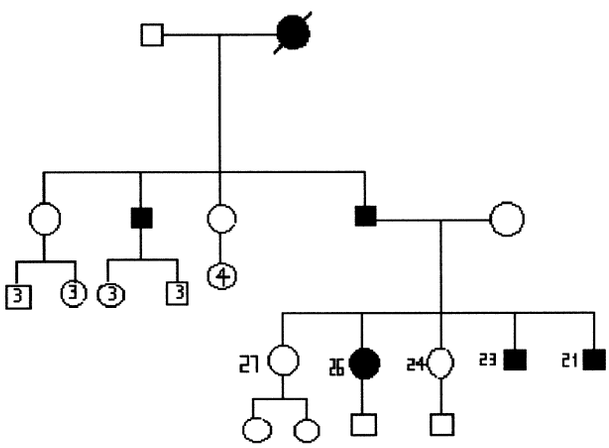

FIG. 1. The pedigree of familial expansile osteolysis (FEO) shows six affected members in three generations. Note that the transmission pattern is suggestive of autosomal-dominant inheritance in this family.

CASE 2

Case 2 was the 15-year-old daughter of Case 1 and the sibling of Case 3. She reported having hearing problems, tinnitus, and vertigo, although no previous evaluations had been done of her. Audiometry revealed a mild, bilateral, conductive hearing loss. Findings of tympanometry were similar to what was found for her father. The result of Rinne testing was negative for both ears. She also had loss of dentition and long-bone pain. Her serum alkaline phosphatase and urinary hydroxyproline levels were elevated. A CT scan in the axial view showed no ossicles in either ear. This patient showed increased uptake and activity at multiple foci of the whole skeleton as well. X-rays showed severe expansion in both the distal end of the femur and the proximal part of the tibia and fibula in addition to coarse trabeculation in the proximal part of the tibia and fibula. Surgical middle ear procedures were performed on this patient under general anesthesia. Visualization of the middle ear in exploratory surgery revealed complete loss of ossicles. The footplate was absent and only the thin membrane was seen; therefore, a small fibrous band replaced them. Therapy consisted of an ossiculoplasty using a total ossicular reconstructive prosthesis (TORP), which was then covered by perichondrium and cartilage. Audiometry performed 4 weeks after surgery indicated no improvement in hearing thresholds. Her parents refused the suggestion of re-surgery. She was referred for fitting with digital hearing aids.

CASE 3

Case 3 was the 11-year-old son of Case 1 and the sibling of Case 2. He reported having hearing loss and

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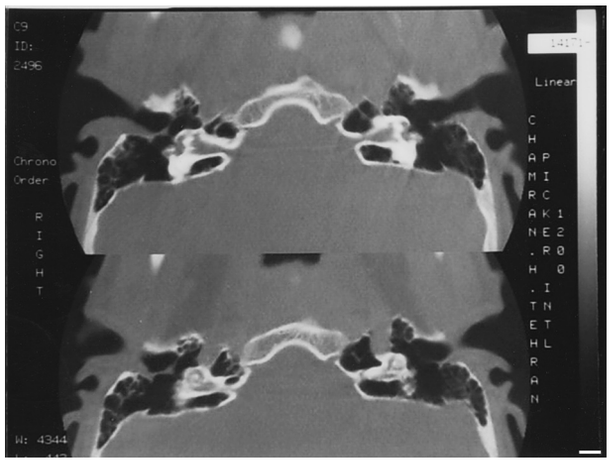

FIG. 2. Case 1. CT scan in the coronal view reveals no ossicles in the middle ear of either ear.

tinnitus in the right ear, but no previous evaluation had been done of him. Audiometry revealed a moderate, bilateral, conductive hearing loss. The results of impedance testing and acoustic reflex were similar to the test results of his father and sister. He also had loss of dentition and long-bone pain. His serum alkaline phosphatase and urinary hydroxyproline levels were elevated. A CT scan in the coronal view showed no ossicles in either ear. Also, whole body isotope scans by Tc-99 mMDP showed increased uptake and activity in multiple foci of the whole skeleton, specifically in the shoulder joint, and sacroiliac area and vertebrae. Exploratory middle-ear surgical findings revealed complete loss of ossicles, so they were replaced with a small fibrous band attachment to the tympanic membrane and promontory. The footplate was absent and only the thin membrane was seen. The same procedure (TORP) accomplished for the Case 2 was used. The audiometry done 4 weeks after surgery indicated no improvement in hearing thresholds of this case as well. His parents refused the suggestion of undergoing surgery again and so he was referred for fitting with digital hearing aids.

DISCUSSION

All obtained data through CT scanning of the temporal bone, biochemical investigation, audiometric evaluations, study of pedigree, whole body isotope scans, x-ray, and exploratory middle ear surgery approved diagnosis of FEO in these cases. All of them had hearing loss due to a total absence of ossicles. Conductive hearing loss in FEO patients reflect structured changes in the ossicles and involvement of the middle ear (1–3). The hearing loss could not be explained by trauma, infection, malformation, or toxic exposure (5). CT scans of all patients showed no ossicles in the middle ear, but did reveal ossicles that had been replaced by fibrous band. Exploratory middle-ear surgical findings revealed the absence of the malleus, the incus, and the stapes. The stapes footplate was absent and only the thin membrane was seen. To our knowledge, the total loss of ossicles has not been reported previously in FEO. Adams et al. (4) reported the otologic manifestations of 19 members within a 50-member family that had been diagnosed with FEO. He had noted common findings in those who had undergone middle-ear surgical procedures: these findings included the replacement of the long process of the incus by a fibrous band in 11 ears; the body of incus was also affected in two of these ears; absence of incus of one ear; abnormality of stapes crura in seven cases; abnormality of stapes footplate in five cases; and absence of one footplate. The malleus of none of these patients showed any abnormality (4). But in their study, they didn't refer to the total loss of middle-ear ossicles at all. Our patients showed no ossicles in the middle ear but did reveal ossicles that had been replaced by a fibrous band. The stapes footplate was absent and only the thin membrane was seen. Osterberg et al. (1) described how the stapes footplate was mobile in all Northern Irish FEO patients except for three whose footplates were fixed with an associated incudostapedial joint abnormality. In our study, Case 1 showed moderate to severe mixed hearing loss, Case 2 indicated mild conductive hearing loss and finally Case 3 had a moderate conductive hearing loss. Impedance testing on all three cases indicated a highly compliant middle ear and absence of acoustic reflex. A few authors have reported a conductive hearing loss that gradually progressed to mixed or sensorineural deafness and, ultimately, to total deafness. The type of hearing loss in all affected patients has been reported as conductive. To accomplish ossicular reconstruction, we used a TORP, which was then covered by perichondrium and cartilage. The result was not satisfactory because of the high mobility of the tympanic membrane in the patent eustachian tube. Nevertheless, Esselman et al. (5) have reported that ossiculoplasty was moderately successful (5). Adams et al. (4) have stated that the result of surgery had been disappointing. Likewise, Wallace et al. (2) have reported that surgical treatment of the abnormality has met with very little success.

CONCLUSION

The total absence of middle-ear ossicles can probably be regarded as a new symptom in some cases with FEO. This has not been reported in the literature to date. Ossiculoplasty by TORP for improvement of hearing thresholds in this condition may be unsuccessful; therefore, both surgeons and patients must be completely aware of the probably undesirable results.

Acknowledgment: We wish to acknowledge the kind and helpful assistance of Hossein Najmabadi, Ph.D., of the Karim-Nejad/Najmabadi Genetics Center of Tehran, Iran, for his

involvement in the project and the preparation of this manuscript.

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